DOCKET NO. 289550-122 U\$2

APPL. NO.: 09/837,235

AMDT. UNDER 37 C.F.R. § 1.312 AMDT. DATED May 31, 2005

PAGE 2 OF 7

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing and Status of Claims:

Claims 1-9. (Canceled)

Claim 10. (Previously Presented): An isolated protein having a functional activity selected from the group consisting of an enzymatic activity, an antigen-binding activity, a protein-protein interaction activity, a DNA binding activity, a hormone activity, a receptor activity, a growth factor activity, and any combinations thereof, comprising at least one di-tyrosine cross-link, wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine, and wherein the di-tyrosine cross-linked protein retains at least one functional activity displayed by the protein in the absence of di-tyrosine cross-linking.

Claim 11. (Previously Presented): The protein of claim 10, further comprising at least one amino acid which originates from a point mutation from tyrosine such that the amino acid is not cross-linked under cross-linking conditions.

Claim 12. (Previously Presented): The protein of claim 10, wherein the protein has enhanced stability compared to the same protein in the absence of di-tyrosine cross-linking.

Claim 13. (Previously Presented): The protein of claim 10, wherein the protein is an enzyme, an antibody, a hormone, a growth factor, a receptor, or a fragment of a hormone, a receptor, a growth factor, an enzyme or an antibody.

Claims 14-17. (Canceled)

Claim 18. (Previously Presented): A method for making a stabilized protein, wherein the protein has a functional activity selected from the group consisting of an enzymatic activity, an

US1DOCS 5133145v1

DOCKET NO. 289550-122 US2

APPL. NO.: 09/837,235

AMDT. UNDER 37 C.F.R. § 1.312 AMDT. DATED May 31, 2005

PAGE 3 OF 7

in interaction activity, a DNA binding activity, a

antigen-binding activity, a protein-protein interaction activity, a DNA binding activity, a hormone activity, a receptor activity, a growth factor activity, and any combinations thereof, comprising:

- (a) selecting one or more residue pairs in a polypeptide chain or chains for di-tyrosine cross-linking,
- (b) mutating at least one of the selected residues to tyrosine; and
- (c) cross-linking the residue pairs in the presence of an oxidant;

wherein the di-tyrosine cross-linked protein retains at least one functional activity displayed by the protein in the absence of di-tyrosine cross-linking, and

wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine.

Claim 19. (Previously Presented): The method of claim 18, wherein the di-tyrosine cross-link reaction occurs in the presence of one or more oxidants selected from the group consisting of hydrogen peroxide, oxone, magnesium monoperoxyphthalic acid hexahydrate (MMPP), a photogenerated oxidant, ammonium persulfate, or any combination thereof.

Claim 20. (Previously Presented): The method of claim 19, wherein the di-tyrosine cross-linking is catalyzed by a catalyst selected from the group consisting of polyhistidine, Gly-Gly-His, a metalloporphyrin, a peroxidase or any combination thereof.

Claim 21. (Canceled)

Claim 22. (Previously Presented): The protein of claim 18, wherein the protein is a hormone, a receptor, a growth factor, an enzyme, an antibody, or a fragment of a hormone, a receptor, a growth factor, an enzyme or an antibody.

Claim 23. (Previously Presented): The protein of any of claims 10-13 or 22, wherein the protein is part of a pharmaceutical composition.

DOCKET NO. 289550-122 US2

APPL. NO.: 09/837,235

AMDT. UNDER 37 C.F.R. § 1.312 AMDT. DATED May 31, 2005

PAGE 4 OF 7

Claim 24. (Previously Presented): The protein of claim 23, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier.

Claim 25. (Previously Presented): The protein of claim 23, wherein the pharmaceutical composition is suitable for *in vivo* use in humans.

Claim 26. (Previously Presented): The protein of any of claims 10-13, 22 or 27, wherein the protein is part of a kit.

Claim 27. (Previously Presented): The protein of claim 10, wherein the protein is a chimeric polypeptide comprising a hormone, a receptor, a growth factor, an enzyme, an antibody, or a fragment of an enzyme, a hormone, a growth factor, a receptor, or an antibody.

Claim 28. (Previously Presented): A composition comprising a protein of any of claims 10-13, 22 or 27.

Claim 29. (Previously Presented): The composition of claim 28, wherein the composition is part of a kit.

Claim 30. (Previously Presented): An isolated stabilized protein having a functional activity selected from the group consisting of an enzymatic activity, an antigen-binding activity, a protein-protein interaction activity, a DNA binding activity, a hormone activity, a receptor activity, a growth factor activity, and any combinations thereof, wherein the protein is obtained from a method comprising:

- (a) selecting one or more residue pairs in a protein for di-tyrosine cross-linking.
- (b) mutating at least one of the selected residues to tyrosine;
- (c) isolating the protein; and
- (d) cross-linking tyrosine residue pairs in the presence of an oxidant;

US1DOCS 5133145v1

DOCKET NO. 289550-122 US2

APPL. NO.: 09/837,235 AMDT. UNDER 37 C.F.R. § 1.312 AMDT. DATED May 31, 2005 PAGE 5 OF 7

wherein the di-tyrosine cross-linked protein retains at least one functional activity displayed by the protein in the absence of di-tyrosine cross-linking, and

wherein at least one tyrosine of a di-tyrosine cross-link originates from a point mutation to tyrosine.

Claim 31. (Previously Presented): The protein of claim 30, further comprising at least one amino acid which originates from a point mutation from tyrosine such that the amino acid is not cross-linked under cross-linking conditions.

Claim 32. (Previously Presented): The protein of claim 18 or 30, wherein the protein has enhanced stability compared to the protein in the absence of di-tyrosine cross-linking.

Claim 33. (Previously Presented): The protein of claim 30, wherein the protein is an enzyme, a hormone, a growth factor, a receptor, an antibody, or a fragment of an enzyme, a hormone, a growth factor, a receptor, or an antibody.

Claim 34. (Previously Presented): The protein of claim 30, wherein the di-tyrosine cross-link reaction occurs in the presence of one or more oxidants selected from the group consisting of hydrogen peroxide, oxone, magnesium monoperoxyphthalic acid hexahydrate (MMPP), a photogenerated oxidant, ammonium persulfate, or any combination thereof.

Claim 35. (Previously Presented): The protein of claim 30, wherein the di-tyrosine cross-linking is catalyzed by a catalyst selected from the group consisting of polyhistidine, Gly-Gly-His, a metalloporphyrin, a peroxidase or any combination thereof.

Claim 36. (Previously Presented): The protein of claim 30, wherein the protein is a chimeric polypeptide comprising a hormone, a receptor, a growth factor, an enzyme, or an antibody, or a fragment of an enzyme, a hormone, a growth factor, a receptor, or an antibody.

Claim 37. (Previously Presented): A composition comprising a protein of claim 30 or 36.

APPL. NO.: 09/837,235

AMDT. UNDER 37 C.F.R. § 1.312 AMDT. DATED May 31, 2005

PAGE 6 OF 7

DOCKET NO. 289550-122 US2

Claim 38. (Previously Presented):

A kit comprising the protein of claim 30 or 36.

Claim 39. (Previously Presented):

A kit comprising the composition of claim 37.

Claims 40-51. (Canceled).

Best Avallable Cob,

US1DOCS 5133145v1